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# Prevalence of Chronic Sputum and Associated Factors in Korean **Adults**

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Chronic sputum is a troublesome symptom in many respiratory diseases. The prevalence of chronic sputum varies from 1.2% to 13% according to the country. The purpose of this study was to estimate the prevalence of chronic sputum and to find its associated factors in a general Korean population. We analyzed the data of the Korea National Health and Nutrition Examination Survey 2010 and 2011. A total number of 6,783 subjects aged 40 yr or more were enrolled in this study with 3,002 men and 3,781 women. As a result, the prevalence of chronic sputum was 6.3% (n = 430). Significant risk factors for chronic sputum by multivariate analysis were: age ( $\geq$  70 yr) (odds ratio [OR], 1.954; 95% confidence interval [CI], 1.308-2.917), current smoking (OR, 4.496; 95% CI, 3.001-6.734), chronic obstructive pulmonary disease (COPD) (OR, 1.483; 95% Cl, 1.090-2.018), and tuberculosis (OR, 1.959; 95% Cl, 1.307-2.938). In conclusion, the prevalence of chronic sputum in Korea was in the intermediate range compared with other countries. Smoking is a preventable risk factor identified in this study, and major respiratory diseases, such as COPD and tuberculosis, should be considered in subjects with chronic sputum.

**Keywords:** Chronic Sputum; Prevalence; Associated Factor

#### INTRODUCTION

Chronic sputum is a troublesome symptom that occurs in many respiratory diseases. It is associated with an accelerated decline in lung function, increased hospitalization (1), and an increase in all-cause mortality (2). The prevalence of chronic cough and sputum production consistently augment with increasing airflow limitation (3). A few reports underline that chronic cough and sputum production before airflow obstruction can offer a unique opportunity to identify subjects at risk for chronic obstructive pulmonary disease (COPD) for an early intervention (4). Chronic sputum has been recognized as a result of tobacco smoking and exposure to industrial dusts or fumes. Other causes of chronic sputum include many respiratory diseases, such as COPD, lung cancer, respiratory tract infection, bronchiectasis, etc. (5-7). Prevalence of chronic sputum varies from 1.2 to 13% according to the country (2, 8-10). However, there are a few studies that assess the prevalence and risk factors of chronic sputum production in the general population, but no report about the prevalence and risk factors of chronic sputum in Korea.

This study was planned to estimate the prevalence of chronic sputum and to study its associated factors in a general Korean population aged over 40 yr.

#### **MATERIALS AND METHODS**

### Study design and measurement

This study collected information from the first and second periods of the 5th Korea National Health and Nutrition Examination Survey (KNHANES V) 2010 and 2011. KNHANES is a crosssectional survey that consists of a health interview, a health behavior questionnaire, a health examination, and a nutrition survey for the general population of Korea (11-14). KNHANES subjects include a representative national sample of the Korean population who were selected using a complex, stratified, multistage probability cluster sampling design (12-14). Participants in KNHANES are non-institutionalized civilians. A total of 17,476 people participated in KNHANES V in 2010 and 2011.

Because the spirometry and respiratory questionnaire were not performed on adults aged < 40 yr who participated in the KNHANES (15), the sample for this study was limited to adults aged  $\geq$  40 yr. The subjects eligible for the present study were those who 1) participated in the KNHANES V and aged  $\geq$  40 yr old, 2) had lung function measurements, 3) had a response to the question: "Have you had sputum almost every day at least three consecutive months one year?". Demographic data selected from KNHANES V included age, gender, level of education, occupation, type of house, smoking status, pulmonary function

test, and tuberculosis.

Chronic sputum was defined as daily emission of sputum that lasted for at least 3 months a year, for more than 1 yr (16). Tuberculosis included both current tuberculosis and past history of tuberculosis. Airflow obstruction was defined as a ratio of the forced expiratory volume in 1 second (FEV1) to the forced vital capacity (FVC) less than 0.7, using data from pre-bronchodilator test. COPD was defined as airflow obstruction in persons aged  $\geq 40 \text{ yr}$  (17). The smoking status was classified as never smokers, past smokers or current smokers (< 15 packyears "light smokers," ≥ 15 pack-years "moderate-heavy smokers"). Never smokers were defined as subjects who had never smoked. Past smokers were defined as subjects who stopped smoking at least in the last year, and current smokers were defined as subjects who continued to smoke (10). Age was categorized into four classes. Occupation was classified into seven categories: managers and professionals, clerks, service and sales workers, skilled agricultural, forestry and fishery workers, plant and machine operators and assemblers, elementary occupations, and unemployed.

## Statistical analysis

The data analysis was carried out utilizing SPSS version 18 to estimate the prevalence of chronic sputum and to evaluate the associated factors for chronic sputum. The dummy variable approach was used to derive the odds ratio for each of the variables, which were of categorical nature, such as age, occupation, and education. The dummy variables were prepared considering each of the classification within the variable as a separate "risk factor" and the remaining subjects as "no risk factor." The multivariate analysis was carried out to study the independent association of the factors, which were observed to be significant in the univariate analysis. Differences in pulmonary function parameters between subjects with and without chronic sputum were examined using independent t-test.

#### **Ethics statement**

This investigation was conducted according to the principles expressed in the Declaration of Helsinki. All examination protocols were approved by the institutional review board of the Korea Centers for Disease Control and Prevention (No. 2010-02CON-21-C and No. 2011-02CON-06-C) (11). Informed consent was waived by the board.

#### **RESULTS**

In the 2010-2011 KNHANES V, 9,159 subjects aged  $\geq$  40 yr were included. Among them, 2,317 subjects did not undergo spirometry and 59 were excluded because of missing or inadequate answer to the question for chronic sputum. A total of 6,783 subjects were eligible for the present study: 430 with chronic spu-

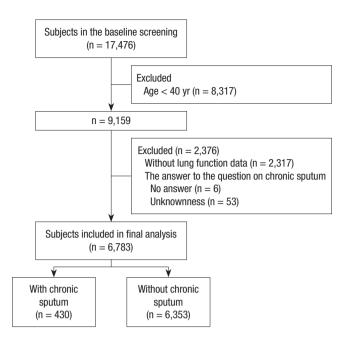


Fig. 1. Selection of the subjects included in this study.

tum, 6,353 without chronic sputum (Fig. 1).

Characteristics of the sample population are presented in Table 1. Of 6,783 participants, 3,002 (44.3%) were men. The mean age of the participants was 57 yr (range: 40-97). More than half of the subjects lived in non-apartment. Most of the males were smokers (2,539, 85.3%), whereas most of the females were never smokers (3,473, 92.5%). Among smokers, moderate to heavy smokers were more than light smokers. The prevalence of COPD was 12.9%, higher in men (21.5%) than in women (6.0%). The number of subjects with current tuberculosis treatment or a history of tuberculosis was 391 (5.8%).

The prevalence of chronic sputum in the population studied was 6.3% (n = 430). Among the subjects with chronic sputum, 24.0% (n = 103) had a chronic cough. The prevalence of sputum and its associated factors are presented in Table 2. The prevalence of chronic sputum was higher in men than in women (OR, 2.517; 95% CI, 2.051-3.089), was positively associated with age ( $\geq$  70 yr) (OR, 1.808; 95% CI, 1.355-2.411), and was higher in both past and current smokers than in never smokers (OR, 1.675; 95% CI, 1.284-2.186, OR, 4.378; 95% CI, 3.489-5.493, respectively), especially in moderate to heavy smokers (OR, 3.488; 95% CI, 2.803-4.340). Also, COPD and tuberculosis were associated with an increased risk of chronic sputum (OR, 2.580; 95% CI, 1.991-3.342, OR, 2.266; 95% CI, 1.650-3.111, respectively). The level of education, occupation, and type of house were not associated with a risk of chronic sputum.

The multivariate logistic regression analysis was carried out to find the independent factors associated with chronic sputum (Table 3), utilizing the factors that were significant in the univariate analysis. Independent association with chronic sputum

Table 1. Characteristics of subjects included in the study

Characteristics		Men		Women		Tota	Total	
Characteristics		(n = 3,002)	%	(n = 3,781)	%	(n = 6,783)	%	
Age (yr)	40-49	881	29.3	1,028	27.2	1,909	28.1	
	50-59	862	28.7	1,201	31.8	2,063	30.4	
	60-69	734	24.5	898	23.8	1,632	24.1	
	≥ 70	525	17.5	654	17.3	1,179	17.4	
Education	Elementary school graduate & under	649	21.9	1,585	42.4	2,234	33.3	
	Middle school graduate	468	15.8	563	15.0	1,031	15.4	
	High school graduate	989	33.3	1,085	29.0	2,074	30.9	
	College graduate	862	29.0	508	13.6	1,370	20.4	
Occupation	Managers, professionals Clerks Service and sales workers Skilled agricultural, forestry & fishery workers Plant and machine operators & assemblers Elementary occupations Unemployed	440 261 208 426 591 251 681	14.9 8.8 10.4 14.4 20.0 8.5 23.0	190 128 567 342 118 472 1,924	5.1 3.4 15.2 9.1 3.2 12.6 51.4	630 389 875 768 709 723 2,605	9.4 5.8 13.1 11.5 10.6 10.8 38.9	
Type of house	Non-apartment	1,676	55.8	2,186	57.8	3,862	56.9	
	Apartment	1,326	44.2	1,595	42.2	2,921	43.1	
Smoking status	Never smoker	436	14.7	3,473	92.5	3,909	58.1	
	Past smoker	1,413	47.5	127	3.4	1,540	22.9	
	Current smoker	1,126	37.8	155	4.1	1,281	19.0	
Amount of smoking	Never	436	14.7	3,473	92.5	3,909	58.1	
	Light	812	27.3	222	5.9	1,034	15.4	
	Moderate- heavy	1,727	58.1	60	1.6	1,787	26.6	
COPD	No	2,026	78.5	3,061	94.0	5,087	87.1	
	Yes	554	21.5	197	6.0	751	12.9	
Tuberculosis	No	2,756	92.6	3,583	95.4	6,339	94.2	
	Yes	219	7.4	172	4.6	391	5.8	

COPD, chronic obstructive pulmonary disease.

was observed for age, COPD, tuberculosis, and smoking, but not for gender. Because odds ratio for chronic sputum increased with age, the older age groups had higher risk. Regarding smoking status, current smoking was a significantly associated factor for chronic sputum.

Pulmonary function parameters between subjects with and without chronic sputum are shown in Table 4. Compared with subjects without chronic sputum, significant reduction of FEV1 (% predicted), FVC (% predicted), and FEV1/FVC ratio were found in subjects with chronic sputum (P < 0.001).

# **DISCUSSION**

The present study evaluated the prevalence of chronic sputum and its associated factors in a general Korean population. The prevalence of chronic sputum was 6.3%. Older age, COPD, tuberculosis, and current smoking were independently associated with chronic sputum. Previous studies from other countries reported that the prevalence of chronic sputum varied from 1.2 to 13% (2, 8-10). In a cross-sectional survey by Mahesh et al. (10), the prevalence of chronic sputum was found to be 1.2% in India, and significant association was observed between chronic sputum, age, and smoking in 4,333 adults aged more than 40 yr living in the rural area of India. In another cross-sectional survey by Cerveri et al. (8), the prevalence of chronic sputum

was 11.9% in Italian people aged between 20-44 yr, and the survey showed that gender (female), smoking, and low socioeconomic status were significantly and independently associated with chronic cough and sputum, with current smoking being the major associated factor. The prevalence of chronic sputum in the present study was in the intermediate range (6.3%) compared with other countries.

Increasing age was found to be an important factor associated with chronic sputum in our study, probably reflecting a higher prevalence of diseases associated with chronic sputum, like bronchiectasis, and a longer duration of exposure to other risk factors. The prevalence of chronic sputum of 8.7% seen in subjects above 70 yr was less than the prevalence observed in another study (2) that included subjects above 65 yr, but more than that in the Indian study (10).

Current smoking was found to be an important association identified in this study for chronic sputum, and both light and moderate to heavy smokers had a higher prevalence of chronic sputum than never smokers. A dose response relationship (association between amount of smoking and chronic sputum) was observed in multivariate analysis, when the amount of smoking was included as a variable (data not shown). Previous studies (8, 10, 18) have demonstrated that smoking is a major risk factor for many respiratory diseases and symptoms with a doseresponse relationship. This supports that smoking is an impor-



Table 2. Associated factors for chronic sputum in the univariate analysis

Variables	Classification	Sputum more than 3 months			
		Prevalence rate (%)	Odds ratio (95% CI)	P value	
Age (yr)	40-49 50-59 60-69 ≥ 70	5.0 6.0 6.6 8.7	1 1.208 (0.918-1.588) 1.325 (0.998-1.760) 1.808 (1.355-2.411)	0.001 0.177 0.052 < 0.001	
Sex	Female Male	3.9 9.4	1 2.517 (2.051-3.089)	< 0.001	
Education	Elementary school graduate & under Middle school graduate High school graduate College graduate	6.8 7.0 5.9 5.8	1 1.028 (0.769-1.375) 0.856 (0.669-1.095) 0.849 (0.642-1.123)	0.419 0.850 0.216 0.253	
Occupation	Managers, professionals Clerks Service and sales workers Skilled agricultural, forestry & fishery workers Plant and machine operators & assemblers Elementary occupations Unemployed	6.3 5.9 5.6 7.8 7.2 6.9 5.8	1 0.927 (0.546-1.574) 0.875 (0.569-1.346) 1.250 (0.826-1.892) 1.143 (0.745-1.755) 1.096 (0.713-1.685) 0.914 (0.638-1.310)	0.414 0.779 0.544 0.292 0.540 0.677 0.624	
Type of house	Non-apartment Apartment	6.4 6.3	1 0.988 (0.811-1.204)	0.906	
Smoking status	Never smoker Past smoker Current smoker	3.7 6.1 14.5	1 1.675 (1.284-2.186) 4.378 (3.489-5.493)	< 0.001 < 0.001 < 0.001	
Amount of smoking	Never Light Moderate-heavy	3.7 6.5 11.9	1 1.786 (1.326-2.405) 3.488 (2.803-4.340)	< 0.001 < 0.001 < 0.001	
COPD	No Yes	5.2 11.9	1 2.580 (1.991-3.342)	< 0.001	
Tuberculosis	No Yes	5.9 12.5	1 2.266 (1.650-3.111)	< 0.001	
Overall		6.3			

CI, confidence interval; COPD, chronic obstructive pulmonary disease.

Table 3. Associated factors for chronic sputum in the multivariate analysis

Variables	Classification -	Sputum more than 3 months			
variables		Multivariate odds ratio (95% CI)	P value		
Age	40-49 50-59 60-69 ≥ 70	1 1.315 (0.962-1.798) 1.349 (0.944-1.928) 1.954 (1.308-2.917)	0.013 0.086 0.100 0.001		
Sex	Female Male	1 1.198 (0.813-1.767)	0.361		
Smoking	Never smoker Past smoker Current smoker	1 1.312 (0.834-2.064) 4.496 (3.001-6.734)	0.241 < 0.001		
COPD	No Yes	1 1.483 (1.090-2.018)	0.012		
Tuberculosis	No Yes	1 1.959 (1.307-2.938)	0.001		

CI, confidence interval; COPD, chronic obstructive pulmonary disease.

tant factor for chronic sputum irrespective of geographical location as well as other smoking-related diseases (10, 19, 20), and that smoking cessation should be encouraged in subjects with chronic sputum to relieve their symptoms.

COPD was significantly associated with chronic sputum. It is well known that chronic sputum is one of common symptoms in COPD (5). Chronic mucus hypersecretion was considered as

Table 4. Pulmonary function parameters according to chronic sputum

Variables	Without chronic sputum, $ {\rm Mean}  \pm  {\rm SD} $	With chronic sputum, Mean $\pm$ SD	P value
FEV <sub>1</sub> , liter	$2.37 \pm 1.07$	$2.28 \pm 1.19$	0.094
FEV <sub>1</sub> , % predicted	$81.73 \pm 32.23$	$74.12 \pm 35.48$	< 0.001
FVC, liter	$3.06 \pm 1.36$	$3.07 \pm 1.58$	0.859
FVC, % predicted	$82.07 \pm 31.8$	$76.36 \pm 35.63$	< 0.001
FEV <sub>1</sub> /FVC ratio	$0.69 \pm 0.26$	$0.62 \pm 0.29$	< 0.001

SD, standard deviation; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity.

a marker of airway inflammation (1, 21). Sputum production has been shown to associate with cellular and structural components of inflammation in COPD (22). Also, it has been considered as an important indicator of respiratory morbidity and mortality. Vestbo et al. (1) reported that chronic cough and sputum production were associated with an excessive FEV1 decline and increased risk of hospitalization because of COPD. These symptoms were associated not only with increased mortality risk (23, 24) but also with exacerbations of COPD (16, 25).

Current tuberculosis or history of tuberculosis was independently associated with chronic sputum in the present study. We speculated that these are probably due to inflammation of respiratory tracts, complication of tuberculosis, such as bronchiectasis (26), extensive pulmonary destruction (26, 27), and chronic pulmonary aspergillosis (28). Other risk factors or diseases can be also responsible for chronic sputum in the community. For instance, underlying respiratory diseases, such as rhinitis, sinusitis, asthma, bronchiectasis, or cystic fibrosis can cause chronic sputum by increasing mucus production (29-31). Moreover, comorbidities such as gastroesophageal reflux, diabetes, cerebrovascular disease, neuromuscular disease can cause chronic sputum by increasing risk of pulmonary aspiration (32, 33). In addition, biomass fuel exposure in rural area is associated with diverse respiratory disease that can cause chronic sputum (34). However, KNHANES V did not obtain enough information about various underlying respiratory diseases and comorbidities. This is one of our study limitations.

Accompanying symptoms of chronic sputum, such as chronic cough, increasing dyspnea, and increased sputum volume/purulence should be investigated, because these symptoms can provide important clinical information about pathology in the bronchopulmonary system (29, 35). However, we could not describe other symptoms except chronic cough, because KN-HANES V did not obtain information about other respiratory symptoms. This is another limitation of this study.

Baseline dermographic characteristics of all subjects aged  $\geq 40$  yr in KNHANES V were similar to those finally included in the present study. In addition, age, tuberculosis, smoking, and COPD were also significant risk factors for chronic sputum when we analyzed the data from all participants in KNHANES V. These results suggest that sample selection bias was not meaningful in this study.

This study has several limitations. First, we could not evaluate all age group because the spirometry and respiratory questionnaire were performed only on adults aged  $\geq 40$  yr. Second, KNHANES V did not obtain enough information about underlying respiratory related diseases, comorbidities, and accompanying symptoms that can be related with chronic sputum as mentioned in the above paragraphs. There is a need for studies to identify more various diseases and factors other than COPD and tuberculosis responsible for chronic sputum in the community. Finally, given the cross-sectional nature of the surveys, we were unable to determine causal relationships between chronic sputum production and other independent variables. Their causal relationship should be verified in future longitudinal studies. Despite these limitations, this study has powerful strength, because the subjects of the current study are representative of the general Korean population.

In conclusion, our findings demonstrate that the prevalence of chronic sputum in the Korean general population is in the intermediate range compared to other countries. Current smoking is an important preventable risk factor identified in this study, and efforts towards smoking cessation are important for respiratory health. Furthermore, major respiratory diseases, such as COPD and tuberculosis, should be considered in subjects with chronic sputum.

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#### **DISCLOSURE**

The authors have no conflicts of interest to disclose.

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#### **REFERENCES**

- 1. Vestbo J, Prescott E, Lange P. Association of chronic mucus hypersecretion with FEV1 decline and chronic obstructive pulmonary disease morbidity: Copenhagen City Heart Study Group. Am J Respir Crit Care Med 1996; 153: 1530-5.
- 2. Enright PL, Kronmal RA, Higgins MW, Schenker MB, Haponik EF. *Prevalence and correlates of respiratory symptoms and disease in the elderly: Cardiovascular Health Study. Chest* 1994; 106: 827-34.
- Anthonisen NR. The British hypothesis revisited. Eur Respir J 2004; 23: 657-8.
- 4. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS; GOLD Scientific Committee. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. Am J Respir Crit Care Med 2001; 163: 1256-76.
- 5. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, Barnes PJ, Fabbri LM, Martinez FJ, Nishimura M, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2013;

187: 347-65.

- 6. Tanaka T, Asai M, Yanagita Y, Nishinakagawa T, Miyamoto N, Kotaki K, Yano Y, Kozu R, Honda S, Senjyu H. Longitudinal study of respiratory function and symptoms in a non-smoking group of long-term officially-acknowledged victims of pollution-related illness. BMC Public Health 2013; 13: 766.
- 7. De Oca MM, Halbert RJ, Lopez MV, Perez-Padilla R, Tálamo C, Moreno D, Muiño A, Jardim JR, Valdivia G, Pertuzé J, et al. *The chronic bronchitis phenotype in subjects with and without COPD: the PLATINO study. Eur Respir J* 2012; 40: 28-36.
- 8. Cerveri I, Accordini S, Corsico A, Zoia MC, Carrozzi L, Cazzoletti L, Beccaria M, Marinoni A, Viegi G, de Marco R. *Chronic cough and phlegm in young adults. Eur Respir J* 2003; 22: 413-7.
- De Marco R, Accordini S, Cerveri I, Corsico A, Antó JM, Künzli N, Janson C, Sunyer J, Jarvis D, Chinn S, et al. *Incidence of chronic obstructive pulmonary disease in a cohort of young adults according to the presence of chronic cough and phlegm. Am J Respir Crit Care Med 2007; 175: 32-9.*
- 10. Mahesh PA, Jayaraj BS, Prabhakar AK, Chaya SK, Vijayasimha R. *Prevalence of chronic cough, chronic phlegm & associated factors in Mysore, Karnataka, India. Indian J Med Res* 2011; 134: 91-100.
- 11. Choi SW, Ryu SY, Han MA, Park J. The association between the socioeconomic status and thyroid cancer prevalence; based on the Korean National Health and Nutrition Examination Survey 2010-2011. J Korean Med Sci 2013; 28: 1734-40.
- 12. Choi CJ, Seo M, Choi WS, Kim KS, Youn SA, Lindsey T, Choi YJ, Kim CM. Relationship between serum 25-hydroxyvitamin D and lung function among Korean adults in Korea National Health and Nutrition Examination Survey (KNHANES), 2008-2010. J Clin Endocrinol Metab 2013; 98: 1703-10.
- 13. Choi KH, Park SM, Park JS, Park JH, Kim KH, Kim MJ. Prevalence of and factors associated with osteoporosis among Korean cancer survivors: a cross-sectional analysis of the Fourth and Fifth Korea National Health and Nutrition Examination Surveys. Asian Pac J Cancer Prev 2013; 14: 4743-50.
- 14. Kim HW, Park H, Cho KH, Han K, Ko BJ. Parathyroid hormone, vitamin D levels and urine albumin excretion in older persons: the 2011 Korea National Health and Nutrition Examination Survey (KNHANES). Clin Endocrinol (Oxf) 2014; 80: 34-40.
- 15. Joo H, Park J, Lee SD, Oh YM. Comorbidities of chronic obstructive pulmonary disease in Koreans: a population-based Study. J Korean Med Sci 2012; 27: 901-6.
- 16. Miravitlles M, Guerrero T, Mayordomo C, Sánchez-Agudo L, Nicolau F, Segú JL. Factors associated with increased risk of exacerbation and hospital admission in a cohort of ambulatory COPD patients: a multiple logistic regression analysis: the EOLO Study Group. Respiration 2000; 67: 495-501.
- 17. Yoo KH, Kim YS, Sheen SS, Park JH, Hwang YI, Kim SH, Yoon HI, Lim SC, Park JY, Park SJ, et al. *Prevalence of chronic obstructive pulmonary disease in Korea: the fourth Korean National Health and Nutrition Examination Survey, 2008. Respirology 2011; 16: 659-65.*
- 18. Bae JM, Lee MS, Shin MH, Kim DH, Li ZM, Ahn YO.  $\it Cigarette\ smoking$

- and risk of lung cancer in Korean men: the Seoul Male Cancer Cohort Study. J Korean Med Sci 2007; 22: 508-12.
- 19. Ahmadi-Motamayel F, Falsafi P, Hayati Z, Rezaei F, Poorolajal J. *Prevalence of oral mucosal lesions in male smokers and nonsmokers. Chonnam Med J* 2013; 49: 65-8.
- Hays JT, Dale LC, Hurt RD, Croghan IT. Trends in smoking-related diseases: why smoking cessation is still the best medicine. Postgrad Med 1998; 104: 56-62, 65-6, 71.
- Lundgren JD, Baraniuk JN. Mucus secretion and inflammation. Pulm Pharmacol 1992; 5: 81-96.
- 22. Saetta M, Finkelstein R, Cosio MG. Morphological and cellular basis for airflow limitation in smokers. Eur Respir J 1994; 7: 1505-15.
- Ekberg-Aronsson M, Pehrsson K, Nilsson JA, Nilsson PM, Löfdahl CG. Mortality in GOLD stages of COPD and its dependence on symptoms of chronic bronchitis. Respir Res 2005; 6: 98.
- 24. Pelkonen M, Notkola IL, Nissinen A, Tukiainen H, Koskela H. Thirty-year cumulative incidence of chronic bronchitis and COPD in relation to 30-year pulmonary function and 40-year mortality: a follow-up in middle-aged rural men. Chest 2006; 130: 1129-37.
- 25. Seemungal TA, Donaldson GC, Paul EA, Bestall JC, Jeffries DJ, Wedzicha JA. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1998; 157: 1418-22.
- Jordan TS, Spencer EM, Davies P. Tuberculosis, bronchiectasis and chronic airflow obstruction. Respirology 2010; 15: 623-8.
- 27. Seddon J, Kasprowicz V, Walker NF, Yuen HM, Sunpath H, Tezera L, Meintjes G, Wilkinson RJ, Bishai WR, Friedland JS, et al. *Procollagen III N-terminal propeptide and desmosine are released by matrix destruction in pulmonary tuberculosis. J Infect Dis* 2013; 208: 1571-9.
- 28. Denning DW, Pleuvry A, Cole DC. Global burden of chronic pulmonary aspergillosis as a sequel to pulmonary tuberculosis. Bull World Health Organ 2011; 89: 864-72.
- 29. Kim WD. Lung mucus: a clinician's view. Eur Respir J 1997; 10: 1914-7.
- 30. Kim C, Kim DG. Bronchiectasis. Tuberc Respir Dis (Seoul) 2012; 73: 249-57.
- 31. Kim HK, Choi EY, Lee JS, Bae YJ, Song JW, Kim TB, Cho YS, Moon HB, Lee SD, Oh YM. Relation between subjective symptoms and rhinolaryngoscopic findings or sputum eosinophilia in chronic cough patients. Tuberc Respir Dis 2010; 69: 368-74.
- DeLegge MH. Aspiration pneumonia: incidence, mortality, and at-risk populations. JPEN J Parenter Enteral Nutr 2002; 26: S19-24.
- 33. Van der Maarel-Wierink CD, Vanobbergen JN, Bronkhorst EM, Schols JM, de Baat C. Risk factors for aspiration pneumonia in frail older people: a systematic literature review. J Am Med Dir Assoc 2011; 12: 344-54.
- 34. Po JY, FitzGerald JM, Carlsten C. Respiratory disease associated with solid biomass fuel exposure in rural women and children: systematic review and meta-analysis. Thorax 2011; 66: 232-9.
- 35. Park S, Lee MG, Lee KH, Park YB, Yoo KH, Park JW, Kim C, Lee YC, Park JS, Kwon YS, et al. *A multicenter study of pertussis infection in adults with coughing in Korea: PCR-based study. Tuberc Respir Dis* 2012; 73: 266-72.